REMARKS

Continued Examination under 37 C.F.R. 1.114

Applicant acknowledges with appreciation that the Examiner entered the Amendments filed on December 18, 2003 and further that all objections and rejections not reiterated in the March 17, 2004 office action have been withdrawn.

Claim Rejections – 35 USC § 112

Claim 84 remains rejected, and claims 73-75, 83 and 98-101 are rejected, under 35 USC § 112, first paragraph. The Examiner states that the specification, while being enabling for the transgenic plants expressing the specific animal viral antigens at the levels set forth in the working examples, does not reasonably provide enablement for expressing in all plants recombinant viral antigen proteins obtained from all animal viruses.

Applicant appreciates the fact that the Examiner acknowledges the specification being enabling for the transgenic plants expressing the specific antigens of the two animal viruses set forth in the working example. Claims 102-104 are added to reflect this consensus between the Examiner and Applicant. Applicant respectfully requests consideration and allowance of these new claims.

With respect to claims 83, 84, 73-75, and 98-101, Applicant submits that the specification is enabling for achieving the levels of expression necessary to elicit an immune response in an animal upon consumption as exemplified in the examples and the detailed teaching of the specification. The Examiner contends that the level of expression of different recombinant proteins in transgenic plants is affected by multiple variables and is thus unpredictable. In

support of the conclusion, the Examiner cites the effects of promoter usage, mRNA stability and codon usage, and recombinant protein stability in plant cells on the levels of accumulation of recombinant proteins in particular transgenic plants. Applicant respectfully disagrees with the Examiner on the issue of enablement.

In assessing whether working examples are sufficient for a claimed genus, MPEP Patent Office Rules and Practice § 2164.02 states,

> For a claimed genus, representative examples together with a statement applicable to the genus as a whole will ordinarily be sufficient if one skilled in the art (in view of level of skill, state of the art and the information in the specification) would expect the claimed genus could be used in that manner without undue experimentation. Proof of enablement will be required for other members of the claimed genus only where adequate reasons are advanced by the examiner to establish that a person skilled in the art could not use the genus as a whole without undue experimentation.

The instant specification clearly has representative, enabling examples in the hepatitis B surface antigen and the TGEV S protein. Additionally, Applicant has provided a list of candidate antigens from various sources in the specification (Pages 21-22). For one skilled in the pertinent art, i.e. transgenic plant production, the claimed invention can be practiced in the manner disclosed without undue experimentation. The various factors raised by the Examiner as affecting the expression levels of recombinant proteins in transgenic plants were known variables to plant molecular biologists at the time of filing of this application. These factors were routinely taken into account in an experimental design for transgenic plant production of recombinant proteins. It's also a known fact that for transgenic plant production of recombinant proteins, it's always necessary to generate a large population of transgenic plants from which a high producer of the recombinant protein is selected. This selection process inevitably involves the working of the various factors raised by the Examiner. Therefore, it cannot be said that the variables the

Examiner set forth would make the instant claims unpredictable or practiced with undue experimentation.

Applicant also respectfully directs the Examiner's attention to another successful example of expression in plants of HIV-related proteins (U.S. Patent Application No. 20040040061). The production of these HIV related surface protein in plants is carried out in roughly the same manner as those disclosed in the instant specification. Yet another successful example of expression of antigens in plants is shown in U.S. Patent Application 200475441 which shows the successful expression of fish antigens in plants, including, avidin and infectious pancreatic necrosis virus VP2 and VP3 using the methods of this invention. This confirms Applicant's belief that the instant specification is enabling to the expression of other viral antigens in view of the level of skill, state of the art, and the information in the disclosure. Applicant respectfully requests the Examiner to withdraw this rejection.

Claim rejection under 35 USC § 112 second paragraph

Claim 100 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to point out and distinctly claim the subject matter which the Applicant regards as the invention. The Examiner contends that it is unclear where or in what context the mucosal immune response occurs. Applicant has amended claim 100 to clearly indicate that the mucosal immune response occurs in a human or other animal.

Claim rejections – 35 USC § 102

Claims 73-75 and 98-100 remain rejected, and claims 83-84 and 101 are rejected, under 35 USC 102(e) as being anticipated by Goodman et al. (U.S. Patent 4,956,282). The Examiner contends

that the physiologically active proteins disclosed in Goodman et al. encompass the antigenic proteins in the instant claims. Applicant respectfully disagrees.

The physiologically active proteins as contemplated by the Goodman reference are proteins that serve a biological function within the organism that produces that protein. These proteins, when produced in transformed cells, are intended to retain the biological activities as those of their native counterparts (column 3, lines 11-30). Thus, a host of mammalian functional proteins including interferons (which is the only example exemplified) and immunoglobulins are proposed for transgenic plant production. These proteins are then administered to animals for their inherent biological functions, not their antigenic properties. The inclusion of viral antigen proteins in the list of candidates for transgenic plant production does not on its face suggest the production of antigens for use as vaccines. As is well known, many of the viral proteins were named as *antigens* because of their initial discovery during immunological screening of animal subjects. In fact, many of the viral antigen proteins serve a distinct function in the proliferation of the viral particle and the interaction between the virus and the host cell. For example, the Simian virus 40 large T antigen interacts with the tumor suppressor p53 and the transcriptional coactivators CBP and p300 in the regulation of cell proliferation and tumerogenesis (Poulin et al., p53 targets Simian virus 40 large T antigen for acetylation by CBP. *J. Virol.* (2004) 78(15): 8245-53). The mere tag of *antigen* to the name of the protein should not be misinterpreted in such a way as to indicate that particular protein is only serving to be an antigen. It is in this context that the viral antigens disclosed in the cited reference should be viewed. The Goodman reference contemplates the transgenic plant production of a host of mammalian proteins, including some viral antigen proteins, in their physiologically active state. These proteins are not disclosed to constitute a vaccine, which distinguishes from the instant claims.

Additionally, "physiological activity" is typically synonymous with the words "biological activity." And the biological activity of a given protein can be maintained when the antigenicity of the same protein is changed. To evade the antibody pressures of the host cells, the influenza A/H3N2 virus changes the antigenicity of hemagglutinin by adding new oligosaccharides to the polypeptide without changing its biological activity (Abe et al., supra). It is therefore evident that a physiologically active protein as disclosed in the Goodman reference is different from an antigen protein disclosed in this invention for the purpose of making a vaccine.

Applicant's view about the Goodman reference is bolstered by a decision by the Board of Patent Appeals and Interferences (*Ex parte* Roy Curtis III and Guy A. Cardineau, Appeal No. 93-4341, Heard January 11, 1996). The Board explicitly stated that the Goodman reference does not teach a transgenic plant which expresses an antigenic protein, and said protein induces an immune response in animals. It is apparent that the Board viewed the Goodman reference as teaching a transgenic plant to function as mini-factory for the production of mammalian proteins, the function of which does not extend to the area of eliciting immune responses in animals. The Board held:

> Where the product can have a physiological effect on ingestion, Goodman discloses, it may be sufficient that the product be retained within the plant. This will be true where the plant part is edible. See Goodman, paragraph bridging pages 9 and 10. However, Goodman does not disclose or suggest retaining in the plant a protein which has no effect on ingestion. Like all of the references discussed above, **Goodman does not disclose or suggest a transgenic plant which (a) expresses a DNA sequence coding for a coloniozation antigen or antigenic determinant thereof, or Streptococcus mutans of Escherichia coli, and (b) induces a secretory iummune response.** (emphasis added)

Because the proteins disclosed in the instant invention and the cited reference can be distinguished structurally and functionally, it cannot be said that the cited reference anticipates the instant claims, which relates to a method of producing a vaccine.

Goodman also only exemplifies the dicot, tobacco to support its disclosures. Monocots are not exemplified. This ultimately resulted in the claims being limited to dicots. For this and other reasons, therefore, the rejection under 35 U.S.C. 102(b) should be withdrawn.

Based on the foregoing, it is apparent that the instant claims are patentably distinguishable from the cited reference. The rejection under 35 U.S.C. 102(b) should be withdrawn.

CONCLUSION

This is a request under the provisions of 37 CFR 1.136(a) to extend the period for filing a response in the above identified application for three months from June 17, 2004 to September 17, 2004. Applicant is a small entity, therefore, please charge Deposit Account Number 26-0084 in the amount of $475.00 for three months to cover the cost of the extension. Any deficiency or overpayment should be charged or credited to Deposit Account 26-0084.

Reconsideration and allowance is respectfully requested.

Respectfully submitted,

LILA A. T. AKRAD, Registration No. 52,550
McKee, Voorhees & Sease, P.L.C.
801 Grand Avenue, Suite 3200
Des Moines, Iowa 50309-2721
Phone No. (515) 288-3667
Fax No. (515) 288-1338
Customer NO: 22885

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